REMARKS

Applicant requests reconsideration in view of the foregoing claim amendments and the remarks that follow.

Status of the claims

Claims 1-12 were pending in the subject application. Claims 11 and 12 have been withdrawn from consideration by the PTO. Claims 1-10 are rejected.

Claim amendments

Applicant has amended claim 1 to address the section 112 issues. These amendments are believed to advance prosecution and place the pending claims in a better form for appeal or allowance.

The Office Action

A. Election/Restriction

As far as the Applicant can understand the Office Action, the PTO has disregarded Applicant's response **with traverse** to the restriction requirement. Thus, the PTO's commentary on page 2 of the Office Action contradict the Applicant's response. Applicant wants to clarify for the record that their election of Group I, claims 1-10 was indeed made with traverse. Proper correction is respectfully requested.

B. Claim objections under 35 U.S.C. § 112

(a) Written Description

Claims 1 is rejected under 35 U.S.C. § 112, first paragraph for allegedly failing to comply with the written description requirement. Specifically, the PTO objects to the phrase "wherein said microemulsion is a system of water, oil, and amphiphile which is a single optically isotropic and thermodynamically stable liquid solution" as lacking support in the specification and thus constitutes new matter.

Applicant has amended claim 1 to delete the phrase, "which is a single optically isotropic and thermodynamically stable liquid solution." With regards to the phrase "wherein said microemulsion is a system of water, oil, and amphiphile," however, Applicant states that the specification provides ample support for microemulsions comprising the recited components. For example, the specification states that the claimed transdermal delivery system comprises water and water-miscible tetraglycol. See page 4 of published application No. WO 2004/000358. The specification also teaches the inventive system to include at least one ester such as a mono- or di-, or tri-glyceride as the oil phase, and can further include pharmaceutically acceptable emulsifiers. *Id,* paragraph bridging pages 4 and 5.

The working examples teach formulations that include Arlacel 186®, glyceryl oleate, as the emulsifier. Emulsifiers are surfactants which by definition are amphiphilic compounds. The terms "emulsifiers" and "surfactants" are well known in the chemical/biochemical art. In view of the above commentary, a skilled artisan would understand the claimed transdermal system to comprise a microemulsion, which system is composed of oil, water and an amphiphile as claimed.

These remarks address the PTO's rejection and Applicant respectfully requests reconsideration and withdrawal of the same.

(ii) Indefiniteness

Claim 1 is rejected under 35 U.S.C. § 112, second paragraph, as being allegedly indefinite. Applicant has amended the claims to Markush format, to clarify claim language and address this rejection. Reconsideration and withdrawal of the same is respectfully requested.

C. Claim objections under 35 U.S.C. § 102

Claims 1-4 and 6-9 are rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. 2002/0034539 ("Esposito"). Applicant respectfully traverses.

The claimed invention is directed to a transdermal system that comprises water, water-miscible tetraglycol and drug and is in the form of a microemulsion. As described in the

specification, the inventive transdermal system has certain advantages. For example, proteins and polypeptides which are difficult to formulate and deliver transdermally are effectively administered through the skin using the inventive transdermal system. The claimed system allows the formulation of water insoluble drugs without the presence of alcohol generally added to solubilize hydrophobic drug entities. See page 3, 2nd and 3rd paragraphs of published application No. WO 2004/000358. Additionally, there are manufacturing advantages associated with the claimed invention. Esposito does not disclose each and every limitation of claim 1, nor the advantages of the inventive transdermal system. Thus, Esposito does not anticipate the claimed invention.

Esposito teaches a biphasic multicomponent dosage form that includes one or more compounds that alter the partition coefficient of a drug between the oil and water phase. Esposito does not teach a transdermal system that is in the form of a microemulsion as claimed. Reference to the term "microemulsion" within Esposito is in the background section, where Esposito discusses the disadvantages of microemulsion compositions in transdermal drug delivery. For example, Esposito states:

> *"An important limit to these biphasical compositions called "microemulsions" is represented by the necessity of formulating the composition according to definite percentages rate of component substances, ..." "This relative composition, ... defined as 'microemulsion', is essentially* ***not modifiable****..... Permeation rate and absorption of drug is therefore determined by the composition and the possibility of modifying such a rate without changing completely the composition of the microemulsion results virtually not realizable."*

See U.S. Publication No. 2002/0034539.

To correct these deficiencies, Esposito teaches a multicomponent biphasic drug composition that has six components, including a surfactant, co-surfactant and a partition modifying compound. *Id* at para. 13. Although, Esposito discloses the use of tetraglycol in its compositions, tetraglycol is presented as one possible choice for the aqueous phase, in a laundry list of compounds that can also be used as an aqueous component. A skilled artisan,

therefore, would not understand Esposito to teach a transdermal system that is a microemulsion, much less a microemulsion that has tetraglycol.

In fact, there is no teaching in Esposito to suggest that tetraglycol takes part in the formation of a microemulsion, much less any disclosure suggesting that tetraglycol is the preferred aqueous component. Rather, Esposito teaches the use of Lutrol® a polyethylene-polypropylene copolymer as the preferred aqueous component of its composition. The above remarks are further strengthened by the lack of any working examples, in Esposito, for a composition containing tetraglycol.

Esposito, therefore, does not anticipate the inventive transdermal system of claim 1. Claims 2-4 and 6-9 depend from amended claim 1 and incorporate all its limitations. These dependent claims are also not anticipated by Esposito for at least the same reasons mentioned above for claim 1.

The above remarks provide compelling evidence that the claims are not anticipated by Esposito and Applicant respectfully requests reconsideration and withdrawal of this rejection.

D. Claim objections under 35 U.S.C. § 103

(i) Non-obviousness over Esposito in view of Guang Lin

Claim 5 is rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. 2002/0034539 ("Esposito") in view of U.S. Patent No. 5,612,324 ("Guang Lin"). Applicant respectfully disagrees.

As stated above, Esposito does not teach the inventive transdermal system. Guang Lin cited by the PTO to teach a transdermal system comprising a guar-based polymer does not cure the defects in Esposito.

Guang Lin teaches a method for treating acne using a skin formulation that contains a pharmaceutically acceptable carrier. Guang Lin discloses the pharmaceutical carriers to be a "hydroalcoholic" system, with working examples disclosing compositions that contain between 35 – 40 % weight of an alcohol. See col. 4, lines 31-32 and examples 1-7.

Nowhere, does Guang Lin teach a transdermal system that is a microemulsion formed of water, oil and amphiphile (i.e., a non-alcoholic system), as claimed.

Although, Guang Lim discloses the use of guar gums in transdermal formulations, these gums are mentioned in a list of optional components for thickening the composition. In contrast, the guar-based polymer hydroxypropyl guar hydroxypropyltrimonium chloride is added to the inventive microemulsions to solidify the drug containing liquid to a hydrogel without destabilizing the microemulsion. As described in the specification and further supported by the working examples, the guar-based polymer assists in dissolving or solubilizing the active material in a hydrogel form and facilitates their penetration through skin. See page 5 of published application No. WO 2004/000358 and working examples. These advantages are absent in Guang Lin's formulation. Furthermore, the incorporation of guar-based gum in Esposito's formulation would not result in the claimed transdermal system.

Additionally, since claim 5 depends ultimately from claim 1, and incorporates all its limitations. Therefore, claim 5 is patentable and non-obvious over the combined teachings of Esposito and Guang Lin because these references fail to render claim 1 obvious.

Applicant respectfully requests reconsideration and withdrawal of this rejection in view of the above remarks.

(i) Non-obviousness over Esposito in view of Dadey

Claim 10 is rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. 2002/0034539 ("Esposito") in view of U.S. Patent 6,417,237 ("Dadey"). Applicant respectfully disagrees.

Again, Esposito does not teach or suggest the claimed transdermal system and the addition of a non-ionic surfactant such as a sorbitan monooleate as taught by Dadey does not remedy the defects in Esposito. Furthermore, claim 10, ultimately depends from claim 1 and incorporates all its limitations. Claim 10, therefore, is not obvious because the combined teachings of Esposito and Dadey fail to teach the inventive transdermal system.

E. Provisional Nonstatutory Obviousness-Type Double Patenting Rejection

Claims 1-10 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12 of copending Application No. 10/343,008.

Copending application No. 10/343,008 claims a transdermal delivery system for analgesic, anti-pyretic and anti-inflammatory drugs. The disclosed drug delivery system is formed by combining the appropriate drug with water-miscible tetraglycol and water and is in the form of a hydrogel. The '008 application does not require the recited drug delivery system to be in the form of a microemulsion. In contrast, the inventive transdermal system comprises drug, tetraglycol and water is formulated to exist in the form of a microemulsion, which microemulsion is recited to be a system of water, oil and an amphiphile.

Accordingly, the provisional nonstatutory obviousness-type double patenting rejection is improper and should be withdrawn.

CONCLUSION

Having advanced credible grounds for overcoming the issues raised in this Office Action, Applicant submits that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned attorney should any issues that warrant further discussion remain.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, then the Commissioner is authorized to charge the unpaid amount to the above deposit account. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. § 1.136 and authorizes payment of any such extensions fees to the deposit account.

Respectfully submitted,

Date March 22, 2010

By _____

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